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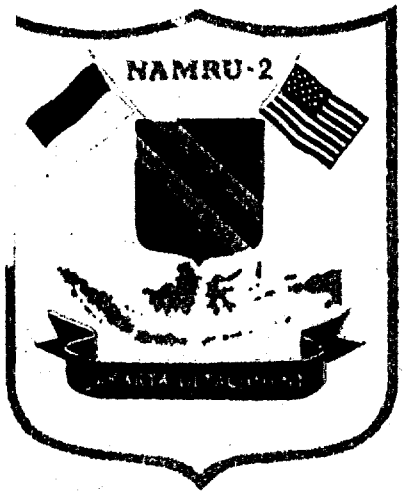

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TOURNIQUET APPLICATION AFTER COBRA BITE: DELAY IN THE ONSET OF NEUROTOXICITY AND THE DANGERS OF SUDDEN RELEASE

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Abstract. The effects of tourniquet application were prospectively studied in 36 hospitalized patients who developed neurotoxic symptoms after bites by the Philippine cobra (*Naja naja philippinensis*). Tourniquets had been applied in 94% of cases and delayed the onset of symptoms. Four patients were asymptomatic prior to the release of their tourniquet and in 11 patients symptoms worsened precipitously. Most importantly, 4 patients developed complete respiratory paralysis requiring artificial ventilation on its removal. Medical personnel seeing patients after a possible cobra bite should remove any tourniquet very gradually with both specific therapy and ventilatory support at hand. We recommend tourniquet application in the Philippines only after the bite of a definitely identified cobra and when removal can take place under controlled hospital conditions.

Fatal respiratory paralysis caused by cobra venom is the leading cause of snakebite death in Southeast Asia,[1–3] including the Philippines.[4] Despite the medical importance of cobra envenoming, no data are available either locally or worldwide on how the outcome of cobra bites is affected by the application of a tourniquet. The use of tourniquets after snakebite is extremely controversial; disagreement results from a lack of data on human snakebite victims[5] and conflicting results from animal studies.[6,7] We therefore prospectively examined the efficacy and dangers of tourniquets in patients envenomed by the Philippine cobra (*Naja naja philippinensis*).

PATIENTS AND METHODS

Patients

All patients who developed neurotoxic signs after a snakebite and who were seen by the principal author were included in the study. Patients were evaluated at 6 different hospitals in Central Luzon Island, Philippines, between March 1984 and March 1987.

Snake identification

Snakes brought to the hospital by patients or their relatives were identified. If the snake was not available for identification, patients and relatives were shown photographs of venomous and nonvenomous Philippine snakes and were carefully questioned about the name and behavior of the snake that had bitten the patient. Blood was collected from each patient on admission for the detection of snake venom antigen by enzyme-linked immunosorbent assay (ELISA) as described by Theakston[8] and Ho.[9] Briefly, rabbits were immunized with crude whole venom from specimens of *N. n. philippinensis* captured on Luzon Island. Eight to 12 mg/ml of IgG were separated from immune rabbit serum with use of a Sepharose protein A column. Two mg of IgG were conjugated to alkaline phosphatase with use of the one-step glutaraldehyde procedure.[10] Plates were coated with 10 μg of the hyperimmune IgG/ml, and a conjugate concentration of 1:500 was used for the final detection of antigen in specimens. Sera from 30 Filipinos who said they had had no previous snakebite served as controls. Tests and control specimens were di-

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luted 1:10 with incubation buffer containing 10% normal human serum and 1% normal rabbit serum to reduce background levels.

Effects of tourniquet application

"Tourniquet" was defined as any broad band or ligature placed proximal to the site of the bite. Patients and their relatives were questioned in detail about the use of a tourniquet and answers were recorded on standardized code sheets. Questions were asked specifically about whether or not a tourniquet was applied, what material was used, how soon after the bite the tourniquet was placed, how long it was left in place, and the effect(s) of its removal on symptoms. Patients were carefully monitored for local swelling and/or necrosis.

RESULTS

Patients

Thirty-one males and 5 females, ranging in age from 16–66 years (mean 33) were included in the study. Sixty-four percent had been bitten below the knee, and 69% of the bites had occurred in a flooded field.

Snake identification

N. n. philippinensis was proven to be the biting species in 30 of 36 cases. Significant amounts of cobra venom antigen were detected in the blood of 24 patients, compared to controls. Values ranged from 10–151 μg/ml (mean 54.8 μg/ml) at a dilution of 1:10. In 2 of these patients and 2 others, the snake was brought to the hospital and identified as *N. n. philippinensis*. Four additional patients reliably identified the biting snake from photographs as a Philippine cobra and saw the snake lift the anterior portion of its body and spread its hood. Philippine cobra bites were strongly suspected in the other 6 cases, since it is the only neurotoxic species of medical importance in the area.[11]

Tourniquet effects

Tourniquets had been applied in 34 of the 36 cases, pieces of clothing being the most common material used. Eleven patients (32%) noted definite sudden exacerbation of neurotoxic symptoms within 10 min after abrupt removal of the tourniquet (Fig. 1B, C). Four additional patients were asymptomatic prior to its removal, but developed symptoms immediately upon its sudden release (Fig. 1A). Respiratory arrest occurred within 10 min of the tourniquet being released in 4 patients, 1 of whom had been asymptomatic (Fig. 1A, B). The tourniquets of 2 patients with mild paralytic symptoms were still in place when these patients were seen by the authors. Pulses distal to the tourniquet were intact. A blood pressure cuff was applied proximally to the tourniquet and inflated to just below systolic blood pressure and the tourniquet then removed. An intravenous infusion of neostigmine methyl sulfate was begun[11] and the cuff then gradually deflated several mm at a time over a period of 30 min. No worsening of symptoms or signs occurred.

The rapidity with which the tourniquet was applied significantly influenced the effects of its removal. Twenty-six patients had a tourniquet placed within 20 min of the bite, and in 15 of these cases symptoms increased upon its removal. Symptoms increased in only 1 of the 8 patients in whom there had been a delay of over 20 min ($P < 0.01$).

One of the 2 patients in whom a tourniquet had not been applied had minor envenoming while the other had gradually progressive respiratory paralysis beginning about 30 min after the bite. Increasingly severe hypoventilation and inability to clear secretions led to hypoxia. The patient became comatose 2 hr after the bite, was seen in a moribund state by the principal investigator 3½ hr after being bitten, and died 15 min later.

Incision and suction had been performed on 4 patients. Symptoms worsened on tourniquet removal in 2 of them and were unchanged in the other 2. In no case was there splinting of the bitten extremity. Only 1 patient developed necrosis, which was clearly related to venom effects rather than to tourniquet application. His tourniquet had been loosely applied, pulses distal to it were noted on admission, and the zone of necrosis was centered at the bite site, far from where the tourniquet had been placed.

DISCUSSION

This study clearly demonstrates that the application of a tourniquet delayed the absorption

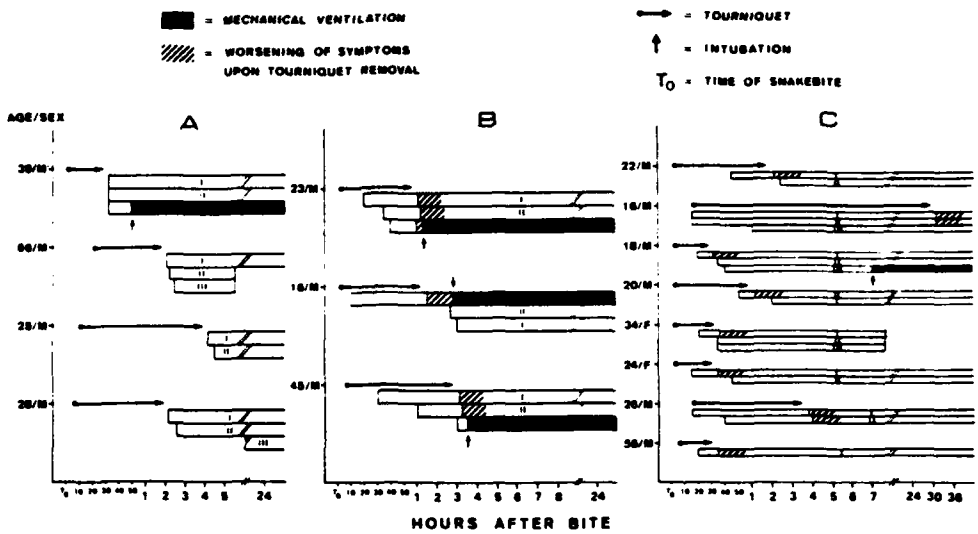

FIGURE 1. Time course of events in three groups of patients after tourniquet removal. A. Symptoms only began after removal. B. Patients had respiratory arrest. C. Symptoms worsened. I = ptosis; II = glossopharyngeal palsy; III = respiratory paralysis.

of cobra neurotoxin(s) into the systemic circulation, and that this effect can have deleterious consequences. Four patients had no symptoms at all prior to its release, and 11 patients' symptoms suddenly worsened. Of greatest consequence, 4 patients developed complete respiratory paralysis on its removal. Tourniquet-induced delay in the progression of symptoms was long lasting. The patient in whom a tourniquet had been left in place the longest, 30 hr, had unequivocable worsening of both ptosis and blurred vision, and more difficulty in swallowing and talking on its release (Fig. 1C, second from top). We speculate that tourniquet removal rapidly released large quantities of neurotoxins into the systemic circulation, where they were then bound en masse to motor endplates. The paralytic effects of cobra venom are dose-dependent.[12]

It is very important therefore that tourniquets not be suddenly released if a cobra bite is suspected, and it is extremely dangerous to do so. Fortunately, facilities for artificial ventilation were available for the 4 patients who developed respiratory paralysis, but this is not always the case in the rural tropics. We have received reports of 2 fatalities occurring in the hospital as a result of abrupt removal of tourniquets, and it is likely that these accidents occur even more often in snakebite victims who don't reach a hospital—the vast majority of cases.[13]

Ischemic necrosis and gangrene are recognized potential complications of a tight-fitting tourniquet,[14, 15] due to compromised blood flow and the retention of venom in the bitten limb.[14, 16, 17] Local tissue damage was not a prominent problem in our patients. Only 8 had swelling extending beyond the bite site and only 1 had necrosis. Tourniquets were most often made from pieces of clothing and were not applied tightly enough to occlude arterial blood flow. One patient did develop necrosis, but it was due to the effects of the venom itself, rather than to the application of a tourniquet. Strips of rubber and tourniquets made from bundles of human hair have been reported to cause necrosis;[5, 14] these materials had not been used in any of our study patients.

Most cobra bites occur in the rural tropics where tourniquets are applied by relatives or friends of the victim, not by medical personnel. Public health recommendations should stress that tourniquets only be applied when the biting snake is known to be a cobra and when the tourniquet can be removed under controlled hospital conditions. These circumstances occur in a small minority of cases, but in these rare instances tourniquet-induced delay in the onset of symp-

toms could be lifesaving. Tourniquets applied to patients not bitten by cobras needlessly expose them to the risks of ischemic tissue damage while a tourniquet applied to a patient not transported to a hospital risks fatal paralysis upon its removal.

Recommendations for other countries may be different. In the United States, tourniquet use is extremely controversial[18] and there are vocal proponents both for[19, 20] and against[21] their use. Release of tourniquets did not lead to a significant rise in venom antigen levels after bites by the Malayan pit viper (*Calloselasma rhodostoma*)[5] in Thailand, while in Burma tourniquets were ineffective in the majority of individuals envenomed by Russell's viper (*Vipera russelli siamensis*).[22] This emphasizes that prospective studies evaluating tourniquets and other first aid measures should be performed in other areas so that rational recommendations regarding their use can be made.

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